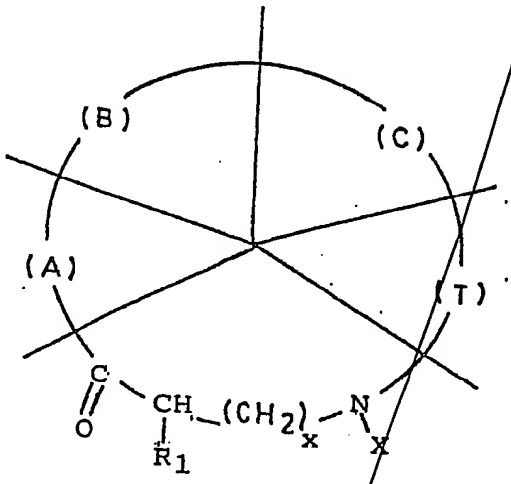
WHAT IS CLAIMED IS:

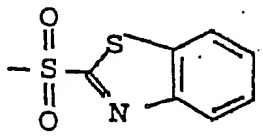
1. A macrocyclic compound of the formula (I)



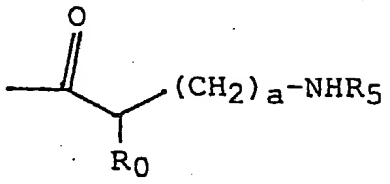
(I)

- where part (A) is a - C - CH - $(CH_2)_y$ - NH - bivalent radical
  O R_2
having its -NH- group linked to the carbonyl group of part - C - CH - $(CH_2)_x$ - N -, a - $(CH_2)_y$ - bivalent radical, or a covalent
  O R_1 X
bond;
- where part(B) is a - C - CH - $(CH_2)_z$ - NH - bivalent radical
  O R_3
having its -NH- group linked to part (A), a - $(CH_2)_z$ - bivalent radical, or a covalent bond;
- where part (C) is a - C - CH - $(CH_2)_t$ - NH - bivalent radical
  O R_4
having its -NH- group linked to part (B), a - $(CH2)_t$ - bivalent radical, or a covalent bond;

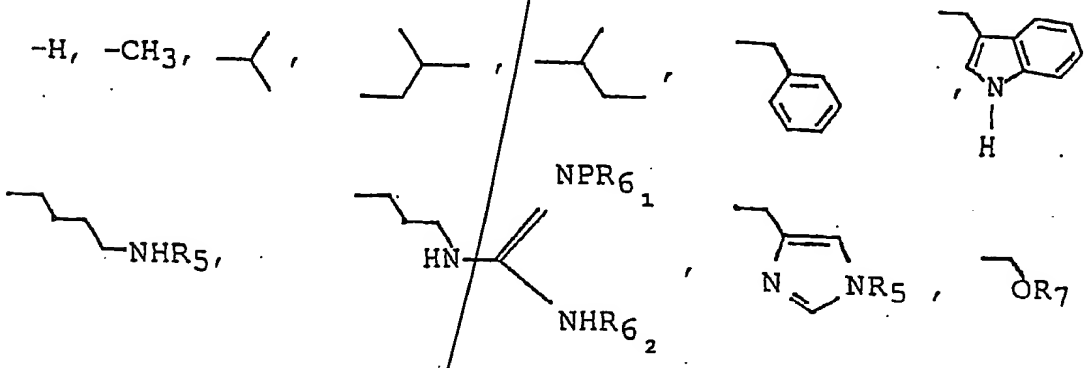
- where part (T) is a - Y - L - Z - radical; and
- where X is a monovalent group selected from the group consisting of: $-SO_2-Ar$, $-SO_2-CH_3$, $-SO_2-CF_3$, -H, -COH, $-CO-CH_3$, -CO-Ar, -CO-R, -CO-NHR, -CO-NHAr, -CO-O-tBu, $-CO-O-CH_2-Ar$

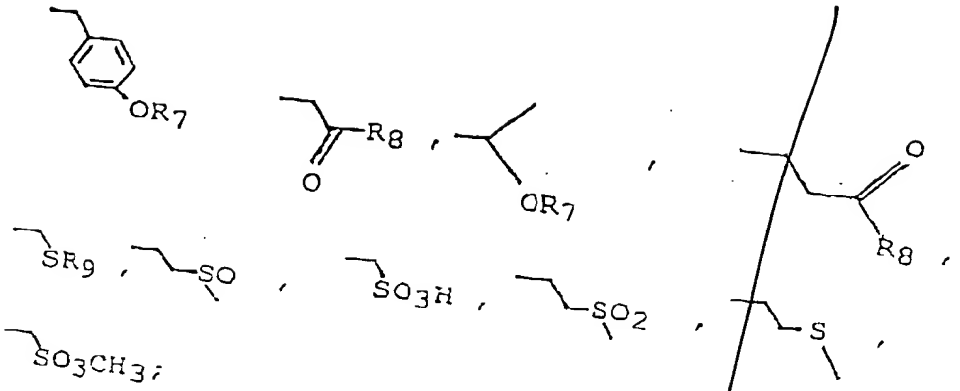


, and



- Ar being an aromatic group, substituted aromatic group or a heteroaromatic group,
- a being an integer selected from the group consisting of 0, 1 and 2,
- R being a monovalent group $-(CH_2)_n-CH_3$ or $-(CH_2)_n-Ar$ with n being an integer from 1 to 16,
- R_0, R_1, R_2, R_3 and R_4 being independently selected from the group consisting of:





proline and hydroxyproline may be used at positions 0, 2 and 3; and 1 when X is CO,

R_5, R_{6_1} and R_{6_2} each being a monovalent radical independantly selected from the group consisting of: -H, $-SO_2-CH_3$, $-SO_2-CF_3$, -COH, $-COCH_3$, -CO-Ar, -CO-R or -CO-NHR wherein R is defined as above, -CONHAr, -COO-tBu and $-COO-CH_2-Ar$, said radical being or not substituted by at least one monovalent group selected in the group consisting of:

$-O-CH_3$, $-CH_3$, $-NO_2$, $-NH_2$, $-NH-CH_3$, $-N(CH_3)_2$, -CO-OH, $-CO-O-CH_3$, $-CO-CH_3$, $-CO-NH_2$, OH, F, Cl, Br and I;

R_7 being a monovalent radical selected from the group consisting of:

-H, -COH, $-CO-CH_3$, NHOH, NHOR, NHR, -CO-R wherein R is defined as above, -CO-Ar and -CO-tBu, said radical being substituted or not by at least one substituent selected from the group consisting of:

$-O-CH_3$, $-CH_3$, $-NO_2$, $-NH_2$, $-NH-CH_3$, $-N(CH_3)_2$, $-CO-OH$, $-CO-O-CH_3$, $-CO-CH_3$, $-CO-NH_2$, OH, F, Cl, Br and I;

R_8 being a monovalent radical selected from the group consisting of: $-OH$, $-NH_2$, $-OCH_3$, $-NHCH_3$, $-O-tBu$ and $-O-CH_2-Ar$, said radical substituted or not by at least one group selected in the group consisting of:

$-O-CH_3$, $-CH_3$, $-NO_2$, $-NH-CH_3$, $-N(CH_3)_2$, $-CO-OH$, $-CO-O-CH_3$, $-CO-CH_3$, $-CO-NH_2$, OH, F, Cl, Br, I;

R_9 being a monovalent radical selected in the group consisting of: -H, -tBu, $-CO-CH_3$, -COAr, -CO-R wherein R is defined as above and -COH, said radicals substituted or not by at least one a monovalent group selected from the group consisting of:

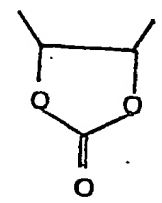
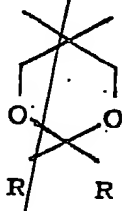
$-O-CH_3$, $-CH_3$, $-NO_2$, $-NH-CH_3$, $-N(CH_3)_2$, $-CO-OH$, $-CO-O-CH_3$, $-CO-CH_3$, $-CO-NH_2$, OH, F, Cl, Br and, I;

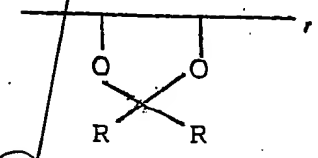
- where Y is a bivalent group $-CH_2-$ or -CO-;
- where Z is a bivalent group -NH- or -O-;
- wherein x, y, z and t are integers each independently selected from the group consisting of 0,1 and 2;
- wherein L is a bivalent radical selected from the group consisting of:

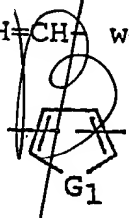
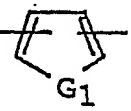
$-(CH_2)_d-A-(CH_2)_j-B-(CH_2)_e-$, d and e being independently an integer from 1 to 5, j being an integer from 0 to 5, when j is 0, A or B is present,

with A and B being independently selected from the group consisting of:

-O-, -NH-, -NR- wherein R is defined as above, -S-, -CO-, -SO-, -CO-O-, -O-CO-, -CO-NH-, -NH-CO-, -SO_2-NH-, -NH-SO_2-,


, -CHOH-,

,


, -CH=CH- with the configuration Z or E, -C≡C-,

G_2 and -G_2-


with the substituent -G_2- in a 1,2, 1,3 or 1,4 position,

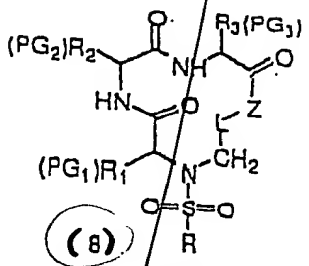
G_1 being selected from the group consisting of:

-O-, -NH-, -NR- wherein R is defined as above, -S-, -CH=CH- with a Z configuration, and -CH=N-; and

G_2 being selected from the group consisting of:

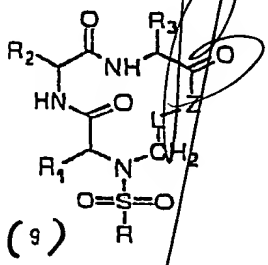
-O-, -NH-, -CO-, -NR- wherein R is defined as above, -CO-O-, -O-CO-, -CO-NH-, -NH-CO-, -SO_2-NH- and -NH-SO_2-.

2. A macrocyclic compound according to claim 1, wherein said compound is of formula (8):



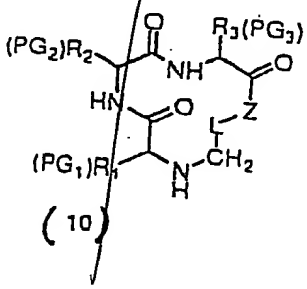
where L, Z, R, R_1, R_2 and R_3 have the same meanings as given in claim 1 and (PG_1), (PG_2) and (PG_3) are protective groups commonly used for orthogonal protections in peptides synthesis.

3. A macrocyclic compound according to claim 1, wherein said compound is of the formula (9):



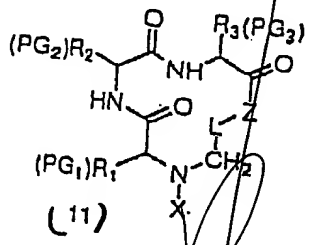
where L, Z, R, R_1, R_2 and R_3 have the same meanings as given in claim 1.

4. A macrocyclic compound according to claim 1, wherein said compound is of the formula (10):



where L, Z, R_1, R_2 and R_3 have the same meanings as given in claim 1 and (PG_1), (PG_2) and (PG_3) are protective group commonly used for orthogonal protection in peptides synthesis.

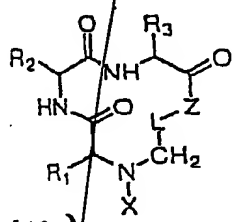
5. A macrocyclic compound according to claim 1, wherein said compound is of the formula (11):



(11)

where L, Z, R_1, R_2 and R_3 have the same meanings as given in claim 1 and wherein (PG_1), (PG_2) and (PG_3) are protective group commonly used for orthogonal protection in peptides synthesis.

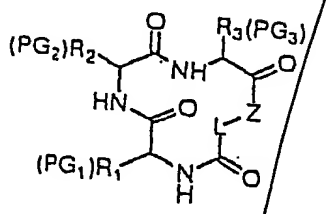
6. A macrocyclic compound according to claim 1, wherein said compound is of the formula (12):



(12)

where L, Z, X, R_1, R_2 and R_3 have the same meanings as given in claim 1.

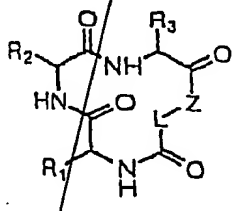
7. A macrocyclic compound according to claim 1, wherein said compound is of the formula (17):



(17)

where X, L, Z, R_1, R_2 and R_3 have the same meanings as given in claim 1 and (PG_1), (PG_2) and (PG_3) are protective group commonly used for orthogonal protection in peptides synthesis.

8. A macrocyclic compound according to claim 1, wherein said compound is of the formula (18):



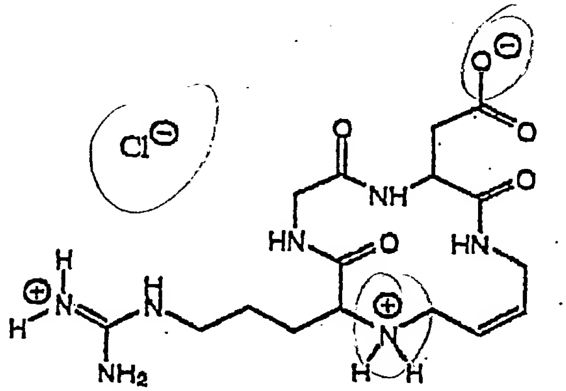
(18)

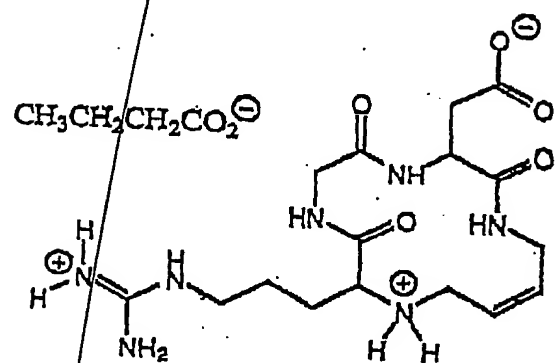
where L, Z, R_1, R_2 and R_3 have the same meanings as given in claim 1.

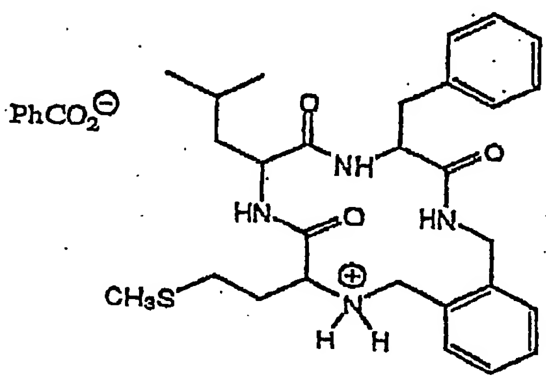
9. A macrocyclic compound according to any one of claims 2, 4, 5 and 7 wherein each of $(PG_1)R_1$, $(PG_2)R_2$, $(PG_3)R_3$,

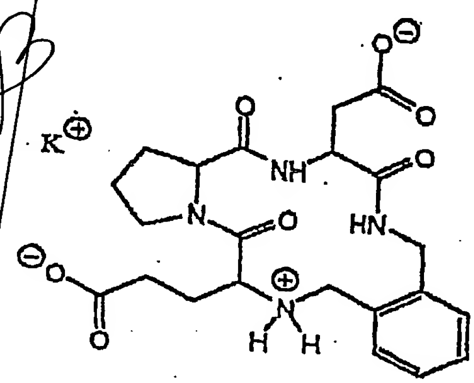
$(PG_4)R_4$ have independently the same meanings as the radical R_5, R_6, R_7, R_8 or R_9 as defined in claim 1.

10. A macrocyclic compound according to claim 1, selected from the group consisting of:

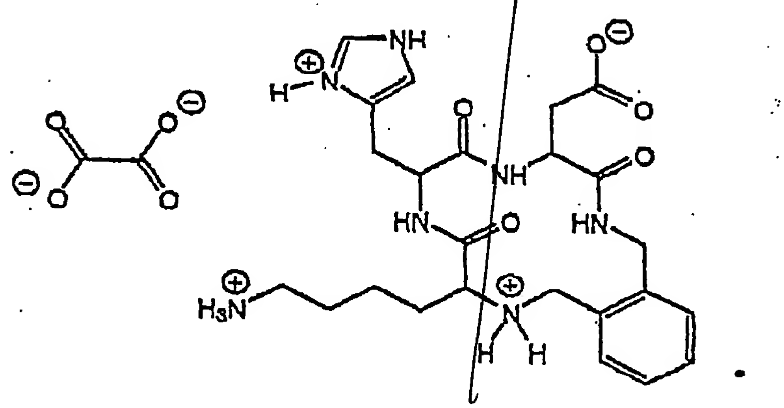






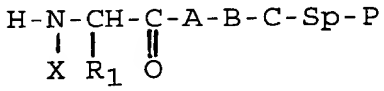


and

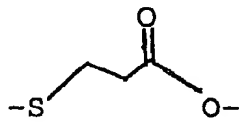
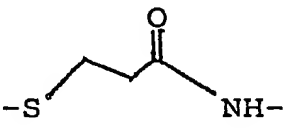


11. A process for preparing a compound of the formula (I) as claimed in claim 1, comprising the steps of:

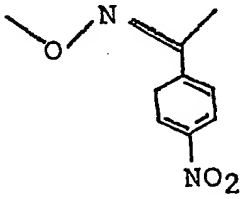
a) preparing by coupling a first building block deriving from natural or synthetic amino-acids, said first building block being of the formula:

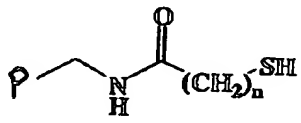


wherein X, R_1, A, B, C are defined as in claim 1,

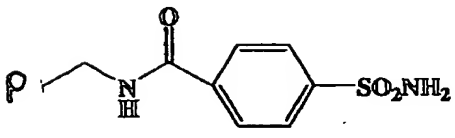
Sp is  or  and

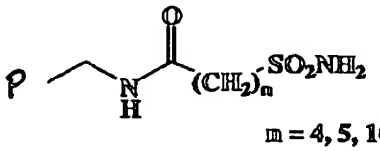
P is $-CH_3$ or $-CH_2$-Ph when the coupling is carried out in liquid phase, and

Sp is 

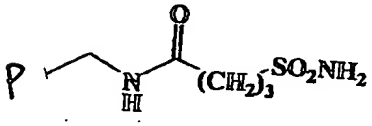


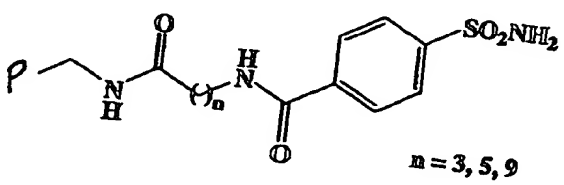
n = 2 (standard), 3, 4, 5, 10





m = 4, 5, 10





n = 3, 5, 9

and P is polystyrene, PEG-polystyrene or polyacrylamide or any suitable resin when the coupling is carried out in solid phase;

b) coupling the first building block prepared in step a) with a second building block hereafter called "tether", of the formula:

$$H\text{-}Y\text{-}L\text{-}Z\text{-}PG_Z$$

wherein Y, L and Z are defined as in claim 1 and PG_Z is a protective group; and

c) removing the protection groups PG_Z from the compound obtained in step b); and

d) carrying out a macrocyclization of the unprotected product obtained in step c) and a cleavage if the above mentioned steps (a) and (b) were carried out in a solid phase, in order to obtain the requested compound of the formula (I).

12. A process according to claim 11, wherein when A, B or C is Arg, the process further comprises the steps of

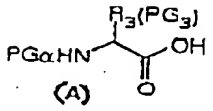
a) utilizing a suitably protected ornithine (Orn) residue as a surrogate for Arg,

b) carrying out a selective deprotection of the protecting on the Orn side chain, and

c) reacting with an appropriately protected guanylating reagent to provide the protected Arg element.

13. A process for preparing a compound of formula (8) as defined in claim 2, comprising the steps of:

a) coupling an amino-acid of the formula A:

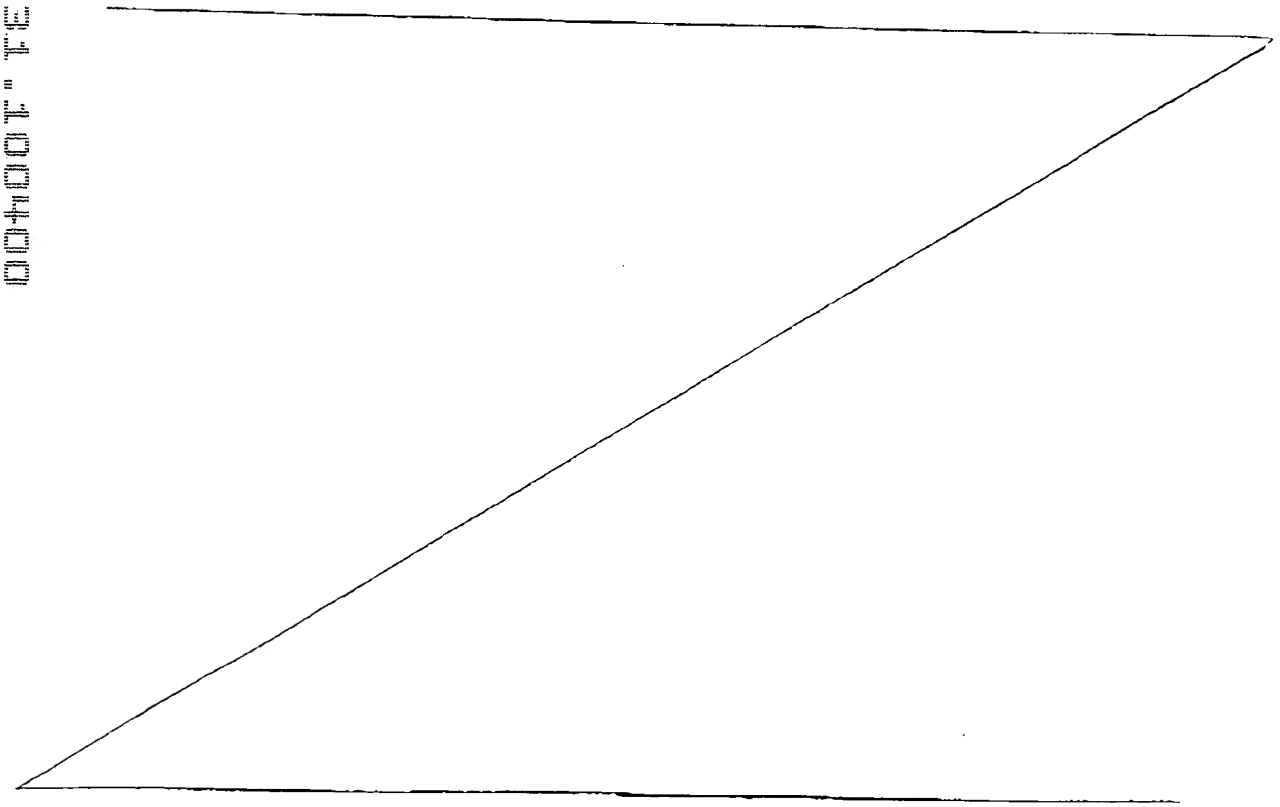


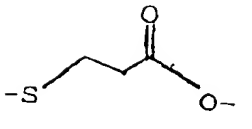
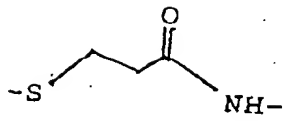
(A)

wherein (PG_α) is an amine protective group and R_3 and PG_3 are defined as in claim 1, either in a solid or a liquid phase, with a compound of the formula:

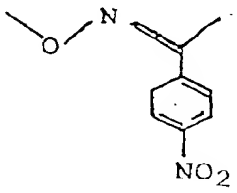
H-Sp-P

wherein, when the coupling is carried out in a liquid phase, Sp is



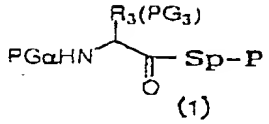



and P is $-CH_3$ or $-CH_2-Ph$ and, when the coupling is carried out in a solid phase, Sp is



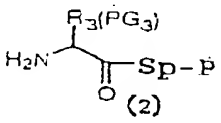
and P is polystyrene,

in order to obtain a compound of the formula (1)



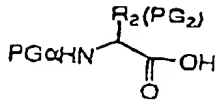
(1)

b) removing the amine protection group PGα from the compound of the formula (1) to obtain the corresponding compound of the formula (2):



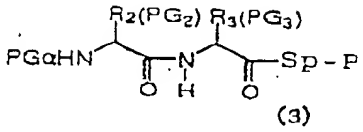
(2)

c) coupling the compound of the formula (2) with another amino-acid of the formula B:



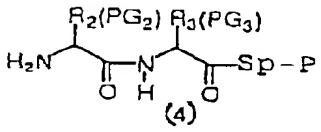
(B)

wherein PGα is defined as above and R_2 and PG_2 are defined as in claim 1, in order to obtain a compound of the formula (3):



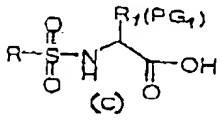
(3)

d) removing the amine protection group PGα from the compound of the formula (3) to obtain the corresponding compound of the formula (4):



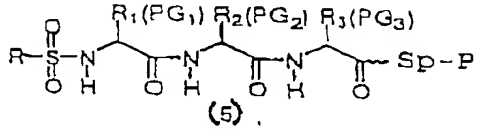
(4)

e) either coupling the compound of the formula (4) with a further amino-acid of the formula (C):



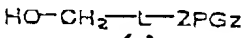
(C)

wherein R is $-(CH_2)_n-CH_3$ or $-(CH_2)_n-Ar$ with n ranging from 1 to 16, in order to obtain a compound of the formula (5):



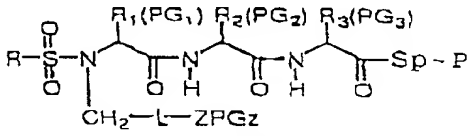
(5)

and coupling said compound of the formula (5) under Mitsunobu conditions with an alchool of the formula (D):



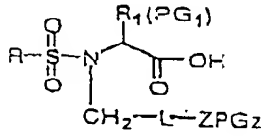
(D)

wherein L and Z are defined as in claim 1 and PG_Z is a protective group, in order to obtain the compound of the formula (6):



(6)

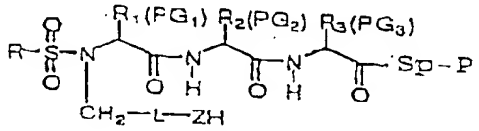
or coupling the compound of the formula (4) with a compound of the formula (E):



(E)

wherein R, L, R_1, PG_1 and PG_2 are defined as above, in order to obtain directly the compound of the formula (6);

f) removing the protective group PG_Z from the compound of the formula (6) to obtain the corresponding compound of the formula (7):



(7)

and

g) carrying out a macrocyclisation of the compound of the formula (7) and a cleavage if the coupling steps were carried out in the solid phase, in order to obtain the requested compound of the formula (8).

14. A process for preparing a compound of the formula (9) as defined in claim 3, which comprises the steps defined in claim 13 and a further step which consists in the removal of the protective group PG1, PG2, PG3 of the compound of formula (8) as defined in claim 12 to yield the requested compound of formula (9).

15. A process for preparing a compound of formula (10) as defined in claim 4, which comprises the steps defined in claim 13 and a further step which consists in the cleaving

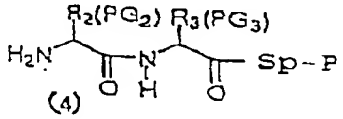
of the sulfonamide portion of the compound of formula (8) to yield the requested compound of formula (10) with a free amine group.

16. A process for preparing a compound of formula (11) as defined in claim 5, which comprises the steps defined in claim 15 and a further step which consists in coupling the free amine of the compound of formula (10) with an acid of formula HX, wherein X has the meaning given in claim 1, to yield the requested compound of formula (11).

17. A process for preparing a compound of formula (12) as defined in claim 6 which comprises the steps defined in claim 16 and a further step which consists in cleaving the orthogonal protecting groups PG1, PG2 and PG3 of the compound of formula (II) to yield the requested compound of formula (12).

18. A process for preparing a compound of formula (17) as defined in claim 7, comprising the steps of:

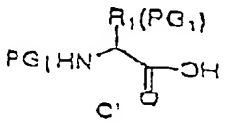
a) coupling an amine of formula (4):



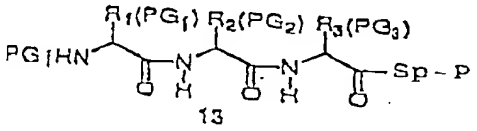
(4)

wherein $R_2(PG_2)$, $R_3(PG_3)$ are protective groups commonly used for orthogonal protection in peptides synthesis, A has the same meaning as given in claim 1, and P is $-CH_3$ or $-CH_2-Ph$ and,

when the coupling is carried out in solid phase, P may also be polystyrene,
with the amino-acid of formula (C'):

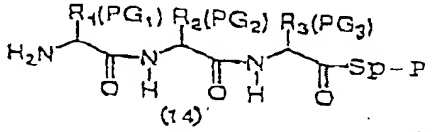


wherein $R_1(PG_1)$ is a protective group commonly used for orthogonal protection in peptides synthesis and wherein PGα is an amine protective group, in order to obtain a compound of formula (13):



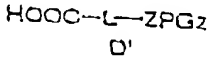
13

b) removing the amino protecting group (PGα) from the compound of formula (13) to obtain the corresponding compound of formula (14):



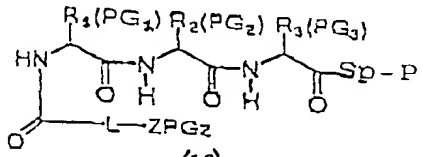
(14)

c) coupling the compound of formula (14) with an hydroxy-acid (Z=O) or with an amino-acid (Z=NH) of formula (D'):



D'

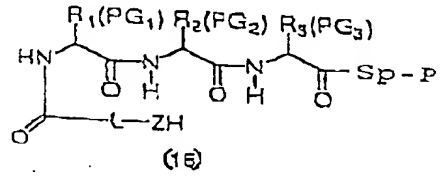
wherein L has the same meaning as in claim 1 and PG_Z is a protective group, to obtain the compound of formula (15):



(15)

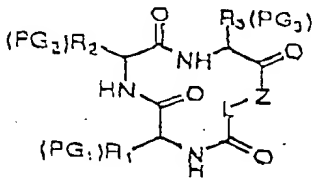
wherein PG_Z is a protective group,

d) removing the terminal alcohol (Z=O) or amine (Z=H) protecting group (PG_Z) from the compound of formula (15) to obtain the corresponding alcohol or amine of the formula (16):



(16)

e) carrying out a macrocyclisation of the compound and a cleaving of formula (16) all at once the compound of formula (16) to obtain the requested compound of formula (17):



(17)

19. A process for preparing a compound of formula (18) as defined in claim 8 which comprises the step defined in claim 17 and a further step of removing the orthogonal protection (PG1), (PG2), (PG3) and (PG4), when a fourth amino-acid is introduced, from the compound of formula (17) to yield to the requested compound of formula (18).

20. A process according to any one of claims 11, 13, 16, 17 and 18, wherein each of $(PG_1)R_1$, $(PG_2)R_2$, $(PG_3)R_3$, $(PG_4)R_4$ and $(PG_z)Z$ have independently the same meanings as the radical R_5, R_6, R_7, R_8 or R_9 as defined in claim 1.

21. A process according to claim 19, wherein at least one of PG_1, PG_2, PG_3, PG_4 and PG_z is a carbamate or a trityl group.

22. A process according to claim 21, wherein the carbamate is selected from the group consisting of Boc, Fmoc and Ddz.

23. A process according to claim 21, wherein the trityl is selected from the group consisting of Trt and Mmt.

Add B27